CONGENITAL MALFORMATIONS IN ISRAEL

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IMPACT OF THE PROBLEM

The interest in congenital malformations increases when the infant mortality rate declines. When the preventable cases decline and form only a small part of the total infant mortality, attention is directed towards the remaining hard-core of infant mortality. At this stage, congenital malformations (CM), which are still to a certain degree a *terra incognita*, gain in importance and are rated at high priority. Infant mortality in Israel declined from 51.7 per 1,000 live births in 1949 to 23.7 in 1964. During these 16 years, the mortality in the second half of infancy (infants aged 6-11 months) diminished to about one-fifth of the 1949 figure; the mortality at the ages 1-5 months declined to less than one-third; even the late neonatal mortality (1-3 weeks) decreased to less than half; but in the first week of life the decrease amounted to only 16.4 per cent. This is the period in which intra-uterine developments influence the mortality rather more than environmental circumstances. Most causes of death showed a more or less regular tendency to decline. But the share of CM in the total infant mortality increased from 9.8 per cent. in 1950 to 21.3 per cent. in 1963 and 20.0 per cent. in 1964. Further improvement in the infant mortality will depend on understanding the biological processes underlying congenital malformations.

CM ranked tenth among causes of death in Israel during 1950-63, when their average rate per 100,000 Jewish population was 16.3. In 1963 there were 285 cases of death among Jews ascribed to CM; only 216 were under one year of age. There were 26 deaths caused by CM per million of population aged 15 and over. The impact of CM is not limited, therefore, to mortality only. In 1962, cases of CM constituted a rate of 159 per 10,000 hospitalizations, excluding deliveries and mental hospitals, and of 195 hospitalization days per 10,000 total days. The average stay

of these cases was almost a fortnight, and the annual total of hospitalization days approaches the 50,000 mark, not including certain categories of CM.

THE PILOT STUDY

Congenital malformations are to a great extent a challenge to paediatrics, and all advanced countries try to discover these cases and follow them up carefully in the hope that a clue to the solution of cause and aetiology may be found. Screening of CM is complicated. Some malformation are unnoticeable at birth and become evident only at a later stage. The way of examination of the newborn and the definition accepted by the examining physician influences the number of registered malformations. Their incidence differs therefore widely in different investigations, depending on the age of examinees, the method of examination, the definition of CM, etc. In the following lines the results are presented of a pilot study of notifications of CM, undertaken in Israel during the two years, 1959 and 1960.

DESCRIPTION OF STUDY

The purpose of the pilot study was to examine how many congenital malformations are recognized by doctors and nurses in the delivery rooms and newborn wards of the hospitals, at birth and during the post-natal hospitalization, and to calculate differential rates of CM. Most deliveries in Israel take place in hospitals. For Jews the percentage is almost 100, with a few exceptional cases delivered at home or on the way to hospital; for non-Jews the proportion is smaller, about 50 per cent. during the years of the study. The post-natal stay of the mother and newborn in hospital is 4-5 days, with a minority staying a week or more. The study applies to CM discovered during this hospitalization period.

We took care not to cause much special work in the hospitals to comply with study requests, which

were therefore minimal. The heads of all maternity departments in the country submitted monthly a list of deliveries in which the infant had a CM. Doctors were asked to notify all conditions which they considered as CM. The list included the name of the mother or her serial number in the hospital, date of delivery, whether live or still birth, and diagnosis of CM. A check on these returns was kept in the Ministry of Health and reminders were issued if a return was not sent in.

At the end of each year a retired graduate nurse with long maternity experience visited all hospitals and reviewed the charts of the relevant cases, according to the monthly returns. She filled out an individual form for each infant born with a CM. This form included particulars routinely available in the chart: age of mother, parity, abortions in reproductive history, ethnic origin, month of births, single or multiple, sex and viability of infant, birth weight, diagnosis of all CMs found in the infant.

During the process of filling out the individual forms inconsistencies were found between the hospital histories and the monthly returns. In certain cases histories could not be found; some charts referred to a completely normal child or a non-maternity, etc. These deficiencies affected almost all institutions, the small peripheral as well as the central, high-standard hospitals.

Two summaries of the material were prepared: in one each malformation was counted separately, while in the other only one—the “main”—malformation was counted for each child, so that the number of malformations corresponded to the number of malformed children. These totals are given in Table I.

Table I shows the complete number of CM reported for Jews during the perinatal period (still births and first week after birth). Among non-Jews it is difficult to assess the accuracy of our figures. For this reason, calculation of rates was feasible only for Jews and only these cases are included in the following discussion, unless otherwise indicated.

TABLE I
SUMMARY OF MATERIAL

No. of Cases	Congenital Malformations	Malformed Infants	Average No. of Malformations per Infant
Total	1,488	1,283	1.16
Ashkenazi* Jews ..	483	429	1.13
Non-Ashkenazi† Jews	895	766	1.17
Non-Jews	110	88	1.25

* European origin.

† Middle Eastern and North African origin.

Because numbers were not great and variation from year to year may cause considerable differences, we dealt with figures for the two years (1959 and 1960) together.

RATES OF MALFORMATION

In calculating crude rates of malformation, we took as numerator the number of malformed infants (Table II).

TABLE II
RATES OF MALFORMATION, BY SEX AND VIABILITY,
1959-60

Viability	Sex	Total number of Births	Malformed Infants	
			Number	Per cent.
Live births ..	M	46,040	665	1.44
	F	43,540	439	1.01
	Total	89,580	1,111*	1.24
Still births ..	M	703	39	5.51
	F	510	44	8.63
	Total	1,213	84†	6.92

* Includes seven infants whose sex was unknown.

† Includes one infant whose sex was unknown.

All differences are significant: between sexes in live births $P < 0.01$ and in still births $P < 0.02$, and between live and still births $P < 0.01$.

As could be expected the rate is considerably higher among still births than among live births. The specific rate by sex is reversed in the two cases: the male rate is higher in live births, whereas the female rate is higher in still births. The average rate of malformation for total births was 1.32 per cent. When multiple births are taken separately, the rate is increased to only 1.43 per cent. (26 malformed infants out of a total of 1,822 born in multiple births).

Age of mother is a factor in the frequency of CM and Table III presents malformation rates by this variable.

TABLE III
RATES OF MALFORMATION, BY AGE OF MOTHER

Age of Mother (yrs)	Total No. of Births	Malformed Infants	
		No.	Per cent.
Less than 20	5,377	60	1.12
20-24	26,797	310	1.16
25-29	28,227	330	1.17
30-34	17,697	262	1.48
35-39	9,490	152	1.60
40-44	2,258	50	2.21
45 and Over	666	6	0.91
Unknown	280	27	9.64
Total	90,792	1,197	1.32

According to the impression of field workers many of the mothers of “unknown” age belong to the

oldest group of 45 years and over. For these two groups combined, the rate of malformation was 3.51 per cent.

Table III shows a steady and persistent rise in the rate of malformed infants with rising age of the mother, three "clusters" of ages being clearly discernible. Up to the age of 29 the malformed infants formed about 1.15 per cent. of the total; for mothers aged between 30 and 39 the percentage rose to 1.5 approximately; for mothers over the age of 40 malformed infants constituted 2 to 3 per cent.

In spite of the fact that age of mother is correlated with parity, the increasing trend of malformations by order of birth is not so clear. Whereas there were births of unknown parity, we calculated the rates of malformations in two ways:

- Excluding the births of unknown parity,
- Dividing them among the groups in proportion to their size. These rates are presented in Table IV.

TABLE IV
RATES OF MALFORMATION, BY PARITY

Parity	Percentage Malformed Infants out of:	
	Infants with Known Parity	All Infants
I	1.30	1.28
II-IV	1.27	1.26
V and Over	1.48	1.46

The differences between the two ways of calculation are negligible, and the differences among the parity groups are not great.

MALFORMED INFANTS

In the Appendix a list of malformed infants reported is presented according to main malformations, coded according to the International Classification of Disease (I.C.D.). Altogether, during the two years, 1,283 malformed infants were born, of whom 88 were non-Jewish. Of the 1,195 Jewish malformed infants, 84 were stillborn, leaving 1,111 liveborn malformed infants during the two years 1959 and 1960. During this period there were 89,580 live births among Jews in Israel, making for a crude rate of 12.4 liveborn malformed infants per 1,000 live births. The small number of cases in many diagnostic categories makes a separate analysis of each item questionable. The only exception in the following analysis is Anencephaly, which was shown separately, although it is included under Monstrosity. The biggest single category was that of infants with a malformation of the extremities, followed by malformations of the external genital

organs, malformations of the heart, other malformations of bone and joint, mongolism, monstrosity, and malformations of the skin. Most of the malformations of the heart were not diagnosed specifically and were therefore included under "Other and Unspecified".

MALFORMATIONS

The total number of malformations reported in the survey was 1,488, of which 110 affected non-Jewish infants. This leaves 1,378 malformations in 1,195 Jewish infants. The average number of enumerated malformations per malformed infant was 1.15 for Jews, 1.25 for non-Jews, and 1.16 for all notified births. 1,130 malformations were notified singly, and 358 appeared in multiple malformations. The total number of infants with multiple malformations was 152, giving an average of 2.36 malformations per infant with multiple malformations.

The ten main groups of malformations quantitatively are enumerated in Table V (opposite).

FINDINGS

We shall analyse some characteristics of mother and infant for selected malformations, the number of which was sufficiently great for a separate analysis.

Age of Mother.—Table VI (opposite) gives rates of malformations per 1,000 births by age of mother.

The significance test is based on the supposition that there is no relation between the age of the mother and the frequency of the specific malformation. Where a significance was found at the 5 per cent. level it was marked +, and at the 1 per cent. level by ++.

Only in two malformations was a significant relation with age found: in mongolism it is highly significant and in "other malformations of bone and joint" it is significant at the 5 per cent. level. In more malformations a trend is evident, although it is not significant. Heart malformations show an increase with the age of the mother which becomes regular in 10-year age groups: 0.56 per 1,000 births in mothers under 20 years of age; 1.33 at ages 20–29; 1.80 at ages 30–39; and 2.39 at ages 40 and over. A similar trend is present in monstrosity and congenital hydrocephalus. The connexion between the incidence of anencephaly and the age of the mother which is evident from the Table is stressed in 10-year age groups: 0.37 per 1,000 births in mothers under 20 years of age; 0.58 at ages 20–29; 0.63 at ages 30–39; and 1.25 at ages 40 and over. These differences are not significant either.

TABLE V
MAIN GROUPS OF MALFORMATIONS BY APPEARANCE

Group	I.C.D. Code	Total No.	Only CM	In association with other CM	
				Main	Other
Mongolism	325·4	97	85	11	1
Extremities	746-749	184	160	6	18
Monstrosity	750	80	61	17	2
Spina bifida and meningocele	751	82	38	23	21
Heart	754·0-754·5	142	106	18	18
Cleft palate and harelip	755	75	55	5	15
Undescended testicle	757·0	72	64	5	3
External genital organs	757·2	147	128	7	12
Other bone and joint	758·6	114	91	6	17
Other and unspecified of skin	759·1	81	69	3	9

TABLE VI
INCIDENCE OF SELECTED MALFORMATIONS, BY AGE OF MOTHER (RATES PER 1,000 BIRTHS)

Malformation	I.C.D. Code	Age of Mother (yrs)							Total*	Significance†
		<20	20-24	25-29	30-34	35-39	40-44	45+*		
Mongolism	325·4	0·37	0·45	0·46	1·07	2·74	7·53	3·19	1·01	++
Extremities	746-749	3·35	1·79	1·77	1·75	1·90	1·77	3·19	1·89	—
Monstrosity	750	0·37	0·52	0·64	0·96	0·53	1·77	2·13	0·68	—
Spina bifida and meningocele	751	0·74	0·56	0·57	1·07	1·05	0·44	2·13	0·74	—
Hydrocephalus, cong.	752	0·56	0·41	0·50	0·68	0·95	1·33	2·13	0·59	—
Heart	754·0-·5	0·56	1·46	1·20	1·81	1·79	2·66	3·19	1·48	—
Cleft palate and harelip	755	0·19	0·86	0·64	1·19	0·53	—	1·06	0·76	—
Undescended testicle	757·0	0·93	0·63	0·99	0·68	0·42	0·89	2·13	0·77	—
External genital organs	757·2	2·05	1·27	1·42	1·53	1·26	1·33	5·32	1·45	—
Other of bone and joint	758·6	0·37	1·31	1·03	1·24	1·37	3·10	3·19	1·22	+
Other of skin	759·1	0·37	0·82	0·92	0·90	0·84	0·89	1·06	0·85	—
Anencephaly‡		0·37	0·49	0·67	0·79	0·32	1·33	1·06	0·61	—

* Including cases of unknown age.

† Excluding cases of unknown age.

‡ Included in Monstrosity.

Parity.—Three categories of malformation showed a significant connexion with parity; the two mentioned in age of mother and also malformations of the extremities. More malformations showed a clear although not significant trend. In malformations of heart and of external genital organs, the incidence declines with increasing parity, whereas in monstrosity, cleft palate and harelip, and other malformations of skin it increases. It seems that a rough division between primiparae and multiparae and even the three-groups division used in Table VII (overleaf) may not be sufficient for studying the

connexion between parity and frequency of malformations. But analysing each parity separately requires accumulation of a large volume of material.

Sex and Viability.—Table VIII (overleaf) combines two variables in their connexion with frequency of malformations: the sex of the infant and its viability, whether born alive or stillborn. The significance of the difference between the sexes was tested separately for liveborn and stillborn infants. The trend was not always parallel.

TABLE VII
INCIDENCE OF SELECTED MALFORMATIONS, BY PARITY (RATES PER 1,000 BIRTHS)

Malformation	I.C.D. Code	Parity				Significance
		I	II-IV	V-	Total	
Mongolism	325·4	0·46	1·09	1·45	1·01	++
Extremities	746-749	2·57	1·57	1·85	1·89	+
Monstrosity	750	0·55	0·60	0·99	0·68	—
Spina bifida and meningocele	751	0·68	0·62	1·04	0·74	—
Hydrocephalus, cong.	752	0·59	0·53	0·72	0·59	—
Heart	754·0-·5	1·56	1·47	1·40	1·48	—
Cleft palate and harelip	755	0·68	0·76	0·86	0·76	—
Undescended testicle	757·0	0·76	0·89	0·54	0·77	—
External genital organs	757·2	1·56	1·51	1·22	1·45	—
Other of bone and joint	758·6	1·01	1·09	1·72	1·22	+
Other of skin	759·1	0·76	0·85	0·95	0·85	—
Anencephaly*		0·55	0·51	0·86	0·61	—

* Included in Monstrosity.

TABLE VIII
INCIDENCE OF SELECTED MALFORMATIONS, PER 1,000 BIRTHS, BY SEX AND VIABILITY OF INFANT

Malformation	I.C.D. Code	Live Births			Still Births			All Births		
		M	F	T*	M	F	T*	M	F	T*
Mongolism	325·4	1·02	0·99	1·00	—	3·92	1·65	1·01	1·02	1·01
Extremities	746-749	1·89	1·88	1·89	—	5·88	2·47	1·86	1·93	1·89
Monstrosity	750	0·13	0·39	0·26	25·60	39·22	32·15	0·51	0·84	0·68
Spina bifida and meningocele	751	0·50	0·73	0·63	9·96	7·84	9·07	0·64	0·82	0·74
Hydrocephalus, cong.	752	0·35	0·39	0·37	17·07	17·65	17·31	0·60	0·59	0·59
Heart	754·0-·5	1·54	1·33	1·47	—	3·92	1·65	1·52	1·36	1·48
Cleft palate and harelip	755	0·67	0·73	0·71	5·69	1·96	4·12	0·75	0·75	0·75
External genital organs	757·2	2·69	0·14	1·46	—	1·96	0·82	2·65	0·16	1·45
Other of bone and joint	758·6	1·35	1·08	1·23	1·42	—	0·82	1·35	1·07	1·22
Other of skin	759·1	0·70	0·99	0·85	—	1·96	0·82	0·68	1·00	0·85
All malformations		16·31	11·62	14·14	79·66	105·88	91·51	17·26	12·71	15·18
Anencephaly†		0·09	0·39	0·23	22·76	35·29	28·03	0·43	0·79	0·61

* Including seven live births and a still birth of unknown sex. † Included in Monstrosity.

Significant differences between the sexes were found in malformations of extremities for still births; in external genital organs the sex difference is highly significant for live births and total births; in monstrosity the significance applies to live births and the total; and for total malformations the difference in live births and in total is highly significant. In the total of CMs the rate for still births is 6·5 times higher than for live births. This difference is only five times for males, whereas it is more than nine

times for females. Out of the ten categories of CM included in Table VIII there were five which did not appear among the 703 male still births, but only one group is not represented among the 510 female still births. The greatest difference between the sexes was in the frequency of malformations of the external genital organs. Also in CMs of the heart and "other malformations of bone and joint" the male rate is higher than the female rate. However, in monstrosity, spina bifida with meningocele, other

CMs of the skin, and CMs of the extremities, the female rates are higher than the male rates. As found elsewhere (*Med. Offr*, 1960) the rate of anencephaly is significantly higher for females than for males in all births ($P < 0.02$) and in live births ($P < 0.01$). The difference is not significant in still births.

As mentioned, the crude rate of CM is considerably higher for still births than for live births. This applies also to most specific malformations. But in malformations of external genital organs and in other malformations of bone and joint the rate of live births is the higher, whereas the rate of other malformations of skin is almost equal in the two cases.

In connexion with viability, a special note is to be made in regard to anencephaly. It is known that anencephalics are rarely born alive and even when liveborn the post-natal existence is limited to a few hours (Record, 1961). In our series the proportion of liveborn anencephalics was 38.2 per cent. for Jews and 18.7 per cent. for non-Jews. This is possibly a consequence of careful registration of infants who die immediately after delivery. Out of 21 Jewish anencephalics born alive, thirteen died during the first 6 hours, and for some the existence was measured in minutes only; three lived 6 to 24

hours and five lived more than 24 hours, two of whom died only after 5 days. The difference between the incidence of anencephaly among live births and still births is significant ($P < 0.01$).

Season of Birth.—The analysis of CMs by season of birth was not done by calculating rates of incidence for each season. Instead, percentages of each quarter in the annual total of cases supply the information (Table IX).

The picture is different for specific malformations. Some are outstanding by the high percentage in the last quarter of the year (undescended testicle, extremities, mongolism). On the other hand, the share of the first quarter is low in undescended testicle, other malformation of skin and of bone and joint, and malformations of heart. A little more than one-third of all "other malformations of bone and joint" occurred in the first half of the year (January–June) whereas 63 per cent. were in the second half. In congenital hydrocephalus there is no great difference between the second and third quarters, but the share of the fourth quarter is greater than that of the first by more than 9 per cent. The difference between these quarters is even greater (almost twice) in other malformations of skin. When

TABLE IX
DISTRIBUTION OF SELECTED CONGENITAL MALFORMATIONS BY SEASON OF BIRTH, 1959–60

Malformation	Month of Birth								Total Cases
	Jan.—March		April–June		July–Sept.		Oct.—Dec.		
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	
Mongolism	22	23·9	19	20·7	19	20·7	32	34·8	92
Extremities	51	29·6	39	22·7	39	22·7	43	25·0	172
Monstrosity	16	25·8	14	22·6	15	24·2	17	27·4	62
Spina bifida and meningocele	18	26·9	17	25·4	17	25·4	15	22·4	67
Hydrocephalus, cong.	11	20·4	13	24·1	14	25·9	16	29·6	54
Heart	26	19·4	37	27·6	38	28·4	33	24·6	134
Cleft palate and harelip ..	14	20·3	19	27·5	17	24·7	19	27·5	69
Undescended testicle	10	14·3	16	22·9	18	25·7	26	37·1	70
External genital organs ..	29	22·0	31	23·5	32	24·2	40	30·3	132
Other of bone and joint ..	20	18·0	21	18·9	36	32·5	34	30·6	111
Other of skin	12	15·5	23	29·9	19	24·7	23	29·9	77
Anencephaly*	16	29·1	11	20·0	11	20·0	17	30·9	55
Total Malformations	314	22·8	344	25·0	352	25·5	368	26·7	1,378
Total Malformed Infants ..	276	23·1	289	24·2	306	25·6	324	27·1	1,195
Total Live Births†		24·9		24·2		26·4		24·5	

* Included in Monstrosity.

† No figures available on the distribution of still births.

compared with the distribution of all live births, only the seasonal distribution of undescended testicle differs significantly. In all other CM the differences and the deviations from the distribution of births are not significant.

A special characteristic of anencephaly mentioned in several studies (*Lancet*, 1960; 1961; 1964; *Brit. med. J.*, 1962) is its winter excess. This is confirmed also in our series, although the seasonal distribution is not significant.

Ethnic Origin.—Unfortunately, we were unable to calculate incidence rates of CMs in the different communities ("edoth") of the Jewish population of Israel. This item is not always accurately recorded in the hospitals, and we had therefore to make the best possible use of the crude distribution into Ashkenazim (*i.e.* European Jews) and non-Ashkenazim (including all communities originating in the Middle East, North Africa, Far East, etc., in spite of the differences among them). The births were divided accordingly on the following assumptions:

- (1) All mothers born in Europe or America were considered Ashkenazi, and those born in Asia and Africa—non-Ashkenazi;
- (2) Mothers born in Israel were divided according to the country of birth of their father;
- (3) The rest, constituting less than 10 per cent., were distributed in the proportion of two-thirds Ashkenazi and one-third non-Ashkenazi.

The difference between the two groups in crude rates was small and not significant.

Ethnic Origin	Ashkenazim	Non-Ashkenazim
Malformed Infants per 1,000 Births	13.70	13.00
Malformations per 1,000 Births	15.35	15.11

The incidence rates for specific malformations were also similar in most cases, and only in three malformations significantly different (Table X).

The frequency of "other malformations of bone and joint" is significantly higher among the non-Ashkenazim, whereas malformations of heart and "other malformations of skin" are significantly more frequent among the Ashkenazim. Among the other CM, although the difference is not significant, it is noticeable that malformations of the central nervous system are more frequent in the non-Ashkenazim. Mongolism is more frequent among the Ashkenazim. The difference in incidence of anencephaly is highly significant ($P < 0.01$). The direction of the difference is opposite to the findings in New York Up-State (Gittelsohn and Milham, 1962), where the incidence among whites was considerably higher than among non-whites.

Multiple Births.—It has already been mentioned that in crude rates there was no significant difference

TABLE X
INCIDENCE OF SELECTED MALFORMATIONS, PER 1,000 BIRTHS, BY ETHNIC ORIGIN

Malformation	Ashkenazim	Non-Ashkenazim	Significance
Mongolism	1.21	0.91	—
Extremities	1.94	1.87	—
Monstrosity	0.54	0.76	—
Spina bifida and meningocele	0.57	0.83	—
Hydrocephalus, cong.	0.48	0.66	—
Heart	1.84	1.28	+
Cleft palate and harelip	0.79	0.74	—
Undescended testicle	0.73	0.79	—
External genital organs	1.49	1.43	—
Other of bone and joint	0.73	1.48	++
Other of skin	1.14	0.69	+
Anencephaly*	0.29	1.21	++

* Included in Monstrosity.

in the rate of malformation among single and multiple births. The situation changes when specific malformations are considered. In most malformations the numbers are too small to be meaningful in regard to multiple births which constitute but 1 per cent. of the total. In those malformations which were found in a "sufficient" number of cases, the high frequency of multiple births is evident. Among 92 cases of mongolism there were three twins; among 172 cases of malformation of extremities there were eight twins, which constitute 5 per cent. of twins in this group of malformed infants as against 1 per cent. in the total infant population; malformation of heart was found in three twins out of a total of 134 cases; there were two twins out of 69 cases with cleft palate and harelip, and two twins among 132 CMs of the external genital organs. Figures are too small to calculate rates and test their significance, but an impression is obtained that CMs are more frequent among infants from multiple births.

Urbanization.—A British study based on data for the years 1944–57 (Pleydell, 1960) found that anencephaly was more frequent in the urban than rural population, in a ratio of 2:1. Density of population is considered to be the real factor, "on the basis of an infectious causation". Our series does not confirm this hypothesis. The ratio of Jewish births in the rural and urban populations is 1:4 approximately, whereas the ratio for cases of anencephaly was only 1:1.75.

DISCUSSION

The literature dealing with different aspects of the problem of congenital malformations is extremely rich, and there is no intention to summarize it or to make extensive comparisons with our series. Some comparisons may help in the evaluation and assessment of our findings and in deciding on future research in this field.

COMPLETENESS OF MATERIAL

Detection of all congenital malformations and the completeness of material are dependent not only on the efforts of the study group. A study group which investigated prenatal handicaps in a group of children (Bierman, Siegel, French, and Connor, 1963) stated that "No matter how careful the appraisal, many congenital defects are not recognizable at birth". Out of 141 children with physical defects only ten were with defects "generally recognizable in the newborn". Not one of the nine children

with suspected mental retardation could be diagnosed in early infancy. Similar results were obtained in other studies in the U.S.A. and in the United Kingdom (Lock, Gatling, and Wells, 1961; McDonald, 1961; McKeown and Record, 1960; *Brit. med. J.*, 1960).

Our data include CMs noted only during the post-natal hospitalization, which lasts on the average 4–5 days. They are not to be considered as a complete record of the incidence of CM. The rate of 13.2 per 1,000 total births found in our study is lower than in Birmingham (McKeown and Record, 1960) and slightly higher than in Japan, in both cases—"soon after birth". This rate is also in near accord with other sources; Prof. M. Lamy reported at a conference (*Brit. med. J.*, 1960) that the "overall incidence of major malformations visible at birth or recognizable by anatomical examination of stillborn infants or infants who die during the neonatal period was close to 1.5 per cent". Our rate is possibly a little lower because anatomical examinations are not always performed on stillborn infants and on those who die in the first few days. Generally, however, some studies have shown lower rates (Poole, 1960, Erhardt and Nelson, 1964, Gentry, Parkhurst, and Bulin, 1959) and others higher rates (Worcester, 1953; Windorfer, 1961).

SINGLE AND MULTIPLE MALFORMATIONS

It has already been mentioned that malformations often appear in association with others. Of the 1,488 malformations included in the present study, only 1,130 appeared singly, leaving 24 per cent. which appeared in association with at least one other (Table XI, overleaf).

With the exception of cleft lip and palate, the percentages of multiple malformations are smaller in Israel than in England, which may be attributed at least partially to deficient recording and to omission of the "less important" malformations from the patient's chart.

PARITY AND MALFORMATIONS

We have already seen that the general connexion between CM and parity is not very clear. There are doubts in this regard in the literature too. Hay (1961) stated that "one writer has suggested that the greatest risk of malformation in the foetus is in the third pregnancy in women over 30 years of age, while another has concluded that there is . . . no consistent association between parity and malformation". The problem is worth further investigation to ascertain whether any association with parity (if

TABLE XI
PERCENTAGE OF MALFORMATIONS ASSOCIATED WITH OTHER MALFORMATIONS

Malformation	McKeown and Record (1960)		Present Study	
	Total Number	Per cent. Multiple	Total Number	Per cent. Multiple
Anencephalus	111	30.6	71	25.4
Spina bifida	166	62.0	82	53.7
Hydrocephalus	140	55.0	63	31.8
Mongolism	88	39.8	97	12.4
Cardiac malformations	224	25.9	142	25.3
Cleft lip and/or palate	105	21.9	75	26.6

present) is independent of association with age, and at which order and for which malformation changes occur.

ANENCEPHALY

On this malformation much research has been done, perhaps because it is easily and reliably identified. There may be truth in the statement (*Med. Offr*, 1960) that "it would seem to the sceptic that only with respect to anencephalus is there likely to be no danger of diagnostic confusion and therefore the differences from country to country in the incidence of this condition are the only ones which can be accepted at their face value".

In spite of this there are very considerable differences in the rates of anencephaly reported: 4.3 per 10,000 live births was reported for Finland and 28.8 for Scotland (*Med. Offr*, 1960); the high prevalence of anencephaly in Iceland (8.6 per 1,000 births) was stressed in comparison with 1.5 in England (*Lancet*, 1961); according to another study (Leck and Millar, 1963), the English rate increased from 1.95 per 1,000 births in 1950-2 to 2.58 in 1957-61; a study for the years 1945-62 in New York State (excluding New York City) gave a rate of 0.81 per 1,000 births (Milham and Gittelsohn, 1965), whereas a study concerned with New York City in 1951 (Wallace, Baumgartner, and Rich, 1953) gave a much lower rate of 0.21 per 1,000 live births. Our rate of 0.61 is lower than most of the above mentioned.

MONGOLISM

The positive association between the age of the mother and the incidence of mongolism is well known, although the exact mechanism behind it is not clear (Erhardt and Nelson, 1964; Worcester, 1953; Milham and Gittelsohn, 1965; *J. Amer. med. Ass.*, 1959; Anderson, Baird, and Thomson, 1958; Beolchini, 1959). This trend is clearly evident and highly significant in our series also (Table VI), the

average incidence being 1.01 per 1,000 births. This is less than that reported from Germany (Oster, 1959) and Great Britain (Pleydell, 1960).

An American gynaecologist (Klebanow, 1948) published data on the frequency of different CMs in several series of Jewish women, who had been interned in Nazi concentration camps; among 1,430 births to such women there were 58 CMs, twelve of them cases of mongolism. Our series included many Ashkenazi women who came to Israel after terrible inhuman experiences in Europe under Nazi rule, but our findings do not support Klebanow's hypothesis.

CONCLUSION

It has been stressed several times in this paper that this survey had a mainly explorative aim of clearing the way for a longitudinal and well-founded programme of collecting and elaborating data on congenital malformations. Two methodological difficulties face any researcher in this field: the duration of observation of the infants and the definition of malformations. With a prolonged period of observation, more malformations will be discovered and recorded. Clear definitions are required, and the doctors and nurses who conduct the observations must know exactly which defects and malformations should be included. Section XIV on "Congenital Malformations" in the International Classification of Diseases (Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, 1957) omits many malformations which appear in other parts of the classification. For example, Mongolism (Code 325.4) is a secondary item under "Mental deficiency" in Section V on "Mental, Psychoneurotic, and Personality Disorders", and Flat foot, Hallux valgus and varus, Clubfoot, and other deformities of the extremities appear in Section XIII on "Diseases of the Bones and Organs of Movement". In all these cases and many more no differentiation is made in

the International Classification between an acquired and a congenital deformity. This makes the collection of data on a broad basis difficult and questionable.

Two publications have suggested modest lists of CM for use in accumulating such data and assuring their uniformity and comparability. The Public Health Conference on Records and Statistics appointed a special Study Group on this topic and its report was published in a mimeographed pamphlet: Report of the Study Group on the Development of Recommendations for Evaluation, Improvement and Utilization of Data on Congenital Malformations from Vital Records (1962); this includes much useful material and may serve as a basis for fruitful discussions. The other deals with the problem from a purely practical point of view and gives well-defined suggestions (Milham, 1963). Both papers based their recommendations on the accepted vital record—birth notification. Complaints by health service workers about the volume of paper work and “exaggerated” requests for statistical data stress the need to avoid additional special reports, and one should try to gain the good-will of field workers by requesting a minimum of extra effort. It is to be hoped that any workable suggestion in this direction will be willingly accepted by research workers as it will contribute to the value and quality of the study of congenital malformations.

Thanks are due to the directors of hospitals and to the doctors and nurses in obstetrical wards who co-operated during 1959–60 in the pilot study by submitting monthly returns and enabling us to collate the data from hospital histories.

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[Appendix overleaf, pp. 76 and 77.]

APPENDIX

MALFORMED INFANTS, BY MAIN CONGENITAL DEFECT

Diagnosis	I.C.D. Code	ALL INFANTS						
		Total (1,283)	Jewish		Non-Jewish (88)	- 19	- 24	- 29
			Ashken- azim (429)	Non-Ashken- azim (766)				
Benign melanoma of skin	220.0	2	—	2	—	—	1	1
Pilonidal cyst	221.0	1	1	—	—	—	1	1
Haemangioma	228.0	3	1	2	—	—	2	1
Other diseases of thyroid gland	234.0	1	—	1	—	—	—	1
Purpura and other haemorrhagic conditions	296.0	2	2	—	—	—	2	—
Mongolism	325.4	96	37	54	5	2	12	13
Amaurosis, congenital	389.1	1	—	1	—	—	1	—
Emphysema, without mention of bronchitis	527.1	1	1	—	—	—	—	1
Hernia, inguinal, congenital	560.0	2	1	1	—	—	—	1
Hernia, umbilical, congenital	560.2	9	5	4	—	—	1	5
Hernia, ventral, congenital	560.3	3	—	3	—	—	1	1
Hernia, of other site, congenital	560.4	4	4	—	—	—	—	2
Hernia, umbilical, with obstruction	561.2	1	—	1	—	—	1	1
Malformation of extremities, congenital	746.9	166	57	99	10	15	41	46
Monstrosity	750	78	17	44	17	2	13	28
Spina bifida and meningocele	751	61	13	39	9	4	12	24
Hydrocephalus, congenital	752	50	11	32	7	2	7	22
Cataract, congenital	753	1	—	1	—	—	—	1
Other malformation of nervous system and sensory organs	753.1	31	5	23	3	1	7	11
Tetralogy of Fallot	754.0	2	2	—	—	1	1	1
Patent ductus arteriosus (Botalli)	754.1	5	2	3	—	—	2	—
Interventricular septal defect	754.2	9	5	4	—	—	5	—
Interauricular septal defect	754.3	2	1	1	—	—	—	1
Fibroelastosis cordis	754.4	1	—	1	—	—	1	—
Other and unspecified malformation of heart	754.5	105	42	55	8	2	25	27
Coarctation of aorta	754.6	1	—	1	—	—	—	1
Cleft palate and harelip	755	60	22	35	3	1	18	16
Hypertrophic pyloric stenosis, congenital	756	1	1	—	—	—	1	—
Imperforate anus	756.1	20	9	11	—	2	3	5
Other malformation of digestive system	756.2	32	11	21	—	2	6	11
Undescended testicle	757.0	69	21	46	2	5	16	27
Polycystic disease of kidney	757.1	5	3	2	—	—	—	3
Congenital malformation of external genital organ	757.2	135	40	80	15	8	33	39
Other malformation of genito-urinary system	757.3	42	17	23	2	6	12	9
Dislocation of hip, congenital	758.0	16	8	8	—	—	3	4
Chondrodystrophy	758.1	11	1	10	—	—	1	1
Malformation of skull, congenital	758.2	6	1	4	1	—	3	2
Brittle bones	758.3	4	2	2	—	—	2	1
Abnormalities of lumbosacral region, congenital	758.5	2	2	—	—	1	1	—
Other congenital malformation of bone and joint	758.6	97	19	77	1	2	30	26
Other congenital malformation of respiratory system	759.0	5	2	3	—	—	1	1
Other congenital malformation of skin	759.1	72	36	33	3	2	19	23
Other congenital malformation of muscle	759.2	9	4	5	—	—	3	3
Other and unspecified malformation	759.3	44	17	25	2	1	16	10
Other birth injury without mention of immaturity	761.0	11	4	7	—	—	4	3
Erythroblastosis without mention of nervous affection or immaturity	770.0	3	1	2	—	1	—	1
Disturbance of co-ordination	780.5	1	1	—	—	—	—	1

MALFORMATION, ISRAEL, 1959-60

JEWISH INFANTS

Mother (yrs)				Parity			Sex and Viability						Birth Weight (g.)					
	-44	45+	?	I	II-IV	V+	Male		Female		?		-1500	-2000	-2500	-3000	3001+	?
							Live	Still	Live	Still	Live	Still						
39	—	—	—	—	1	1	2	—	—	—	—	—	—	—	—	1	1	—
38	—	—	—	—	1	—	1	—	—	—	—	—	—	—	—	—	3	—
37	—	—	—	2	—	1	2	—	1	—	—	—	—	—	—	—	1	—
36	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	2	—
35	17	1	2	11	48	32	46	—	43	2	—	—	1	3	14	32	41	—
34	—	—	—	—	1	—	1	—	—	—	—	—	—	—	—	—	1	—
33	—	1	—	—	1	—	2	—	—	—	—	—	—	—	1	—	1	—
32	—	—	—	—	6	2	5	—	4	—	—	—	—	—	—	3	6	—
31	—	—	—	—	—	2	1	—	2	—	—	—	1	—	—	1	1	—
30	—	—	—	3	1	—	1	—	2	1	—	—	1	—	1	—	—	1
29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
28	2	—	3	60	60	36	79	—	77	—	—	—	1	1	8	46	98	2
27	4	—	2	13	27	21	6	—	17	—	—	—	12	1	9	10	15	3
26	1	—	1	13	20	19	21	—	27	1	—	—	1	5	6	15	23	—
25	2	—	1	9	19	15	11	—	11	10	—	—	1	7	2	13	17	3
24	—	—	—	—	—	1	—	—	1	—	—	—	—	—	—	1	—	—
23	—	1	—	4	10	14	14	—	14	—	—	—	—	3	4	7	14	—
22	—	—	—	2	—	—	1	—	1	—	—	—	—	—	—	1	1	—
21	—	—	—	1	4	—	3	—	1	—	—	—	—	—	2	1	2	—
20	—	—	—	3	—	2	5	—	3	1	—	—	—	—	1	1	7	—
19	—	—	—	—	1	1	1	—	—	—	—	—	—	—	—	—	1	—
18	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—
17	5	1	—	25	50	22	52	—	43	1	1	—	—	1	12	24	59	1
16	—	—	—	14	27	16	27	—	1	—	—	—	—	—	3	12	1	—
15	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	37	—
14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—
13	2	—	—	6	9	5	15	—	4	—	1	—	1	2	—	5	11	1
12	—	—	2	6	19	7	11	—	20	1	—	—	—	1	7	7	15	—
11	—	—	—	17	39	11	67	—	—	—	—	—	—	—	2	18	47	—
10	—	—	—	2	2	2	3	—	2	—	—	—	—	1	1	2	1	—
9	3	—	4	30	63	27	115	—	5	—	—	—	—	4	5	31	80	—
8	1	—	1	7	23	10	38	—	1	1	—	—	—	1	1	4	34	—
7	—	—	—	4	7	5	4	—	12	—	—	—	—	—	1	4	11	—
6	—	—	—	3	4	4	2	1	7	—	—	—	1	—	3	1	4	—
5	—	—	—	—	4	1	3	—	2	—	—	—	—	—	—	1	1	—
4	—	—	—	1	2	—	—	—	1	—	—	—	—	—	1	2	1	—
3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	1	—
2	6	1	—	23	42	31	52	—	44	—	—	—	—	—	10	16	69	—
1	—	—	—	15	4	19	4	—	1	—	—	—	—	—	2	2	1	—
0	2	—	—	3	35	6	26	—	41	1	1	—	1	—	8	14	45	—
—	—	—	—	14	18	10	4	—	4	—	—	—	—	—	—	1	8	—
—	—	—	—	3	5	3	20	—	17	3	—	—	4	3	4	9	22	—
—	—	—	—	1	1	1	9	—	2	—	—	—	—	—	1	2	8	—
—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	1	2	—